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Filed : December 27, 2001

## AMENDMENTS TO THE SPECIFICATION

Please amend the title as follows:

~~SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS~~  
~~ENCODING THE SAME~~ A NUCLEIC ACID AMPLIFIED IN LUNG AND COLON TUMORS

Please replace the paragraph beginning at page 9, line 27 of the substitute specification, with the following rewritten paragraph:

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1800 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 278, inclusive of ~~Figure 2 (SEQ ID NO: 3)~~ Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

Please replace the entire section entitled "BRIEF DESCRIPTION OF THE DRAWINGS" beginning on page 34, line 21 of the substitute specification, with the following rewritten section:

### BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a nucleotide sequence (SEQ ID NO:1) of a native sequence PRO1800 cDNA, wherein SEQ ID NO:1 is a clone designated herein as "DNA35672-2508".

Figure 2 shows the amino acid sequence (SEQ ID NO:2) derived from the coding sequence of SEQ ID NO:1 shown in Figure 1.

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Figure 3 shows a nucleotide sequence (SEQ ID NO:6) of a native sequence PRO539 cDNA, wherein SEQ ID NO:6 is a clone designated herein as "DNA47465-1561".

Figure 4 shows the amino acid sequence (SEQ ID NO:7) derived from the coding sequence of SEQ ID NO:6 shown in Figure 3.

Figure 5 shows a nucleotide sequence (SEQ ID NO:8) of a native sequence PRO982 cDNA, wherein SEQ ID NO:8 is a clone designated herein as "DNA57700-1408".

Figure 6 shows the amino acid sequence (SEQ ID NO:9) derived from the coding sequence of SEQ ID NO:8 shown in Figure 5.

Figure 7 shows a nucleotide sequence (~~SEQ ID NO:12~~SEQ ID NO:10) of a native sequence PRO1434 cDNA, wherein ~~SEQ ID NO:12~~SEQ ID NO:10 is a clone designated herein as "DNA68818-2536".

Figure 8 shows the amino acid sequence (~~SEQ ID NO:13~~SEQ ID NO:11) derived from the coding sequence of ~~SEQ ID NO:12~~SEQ ID NO:10 shown in Figure 7.

Figure 9 shows a nucleotide sequence (~~SEQ ID NO:17~~SEQ ID NO:15) of a native sequence PRO1863 cDNA, wherein ~~SEQ ID NO:17~~SEQ ID NO:15 is a clone designated herein as "DNA59847-2510".

Figure 10 shows the amino acid sequence (~~SEQ ID NO:18~~SEQ ID NO:16) derived from the coding sequence of ~~SEQ ID NO:17~~SEQ ID NO:15 shown in Figure 9.

Figure 11 shows a nucleotide sequence (~~SEQ ID NO:19~~SEQ ID NO:17) of a native sequence PRO1917 cDNA, wherein ~~SEQ ID NO:19~~SEQ ID NO:17 is a clone designated herein as "DNA76400-2528".

Figure 12 shows the amino acid sequence (~~SEQ ID NO:20~~SEQ ID NO:18) derived from the coding sequence of ~~SEQ ID NO:19~~SEQ ID NO:17 shown in Figure 11.

Figure 13 shows a nucleotide sequence (~~SEQ ID NO:21~~SEQ ID NO:19) of a native sequence PRO1868 cDNA, wherein ~~SEQ ID NO:21~~SEQ ID NO:19 is a clone designated herein as "DNA77624-2515".

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Figure 14 shows the amino acid sequence (~~SEQ ID NO:22~~SEQ ID NO:20) derived from the coding sequence of ~~SEQ ID NO:21~~SEQ ID NO:19 shown in Figure 13.

Figure 15 shows a nucleotide sequence (~~SEQ ID NO:23~~SEQ ID NO:21) of a native sequence PRO3434 cDNA, wherein ~~SEQ ID NO:23~~SEQ ID NO:21 is a clone designated herein as "DNA77631-2537".

Figure 16 shows the amino acid sequence (~~SEQ ID NO:24~~SEQ ID NO:22) derived from the coding sequence of ~~SEQ ID NO:23~~SEQ ID NO:21 shown in Figure 15.

Figure 17 shows a nucleotide sequence (~~SEQ ID NO:25~~SEQ ID NO:23) of a native sequence PRO1927 cDNA, wherein ~~SEQ ID NO:25~~SEQ ID NO:23 is a clone designated herein as "DNA82307-2531".

Figure 18 shows the amino acid sequence (~~SEQ ID NO:26~~SEQ ID NO:24) derived from the coding sequence of ~~SEQ ID NO:25~~SEQ ID NO:23 shown in Figure 17.

Please replace the paragraph beginning at page 68, line 37 of the substitute specification, with the following rewritten paragraph:

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1434 (shown in ~~Figure 10 and SEQ ID NO:13~~Figure 8 and SEQ ID NO:11) has certain amino acid sequence identity with the mouse nel protein precursor (NEL\_MOUSE). Accordingly, it is presently believed that PRO1434 disclosed in the present application is a newly identified nel homolog and may possess activity typical of the nel protein family.

Please replace the paragraph beginning at page 69, line 10 of the substitute specification, with the following rewritten paragraph:

Using WU-BLAST2 sequence alignment computer programs, it has been found that amino acids 41 to 487 of PRO1917 (shown in ~~Figure 14 and SEQ ID NO:20~~Figure 12 and SEQ ID NO:18) has certain amino acid sequence identity

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with an inositol phosphatase designated in the Dayhoff database as "AF012714\_1". Accordingly, it is presently believed that PRO1917 disclosed in the present application is a newly identified member of inositol phosphatase family and may possess enzymatic activity typical of inositol phosphatases.

Please replace the paragraph beginning at page 69, line 17 of the substitute specification, with the following rewritten paragraph:

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1868 (shown in ~~Figure 16 and SEQ ID NO:28~~ Figure 14 and SEQ ID NO:20) has certain amino acid sequence identity with the human A33 antigen protein (P\_W14146). Accordingly, it is presently believed that PRO1868 disclosed in the present application is a newly identified A33 antigen homolog which may possess activity and/or expression patterns typical of the A33 antigen protein. The PRO1868 polypeptide may find use in the therapeutic treatment of inflammatory diseases as described above and colorectal cancer.

Please replace the paragraph beginning at page 69, line 31 of the substitute specification, with the following rewritten paragraph:

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1927 (~~Figure 20; SEQ ID NO:26~~ Figure 18; SEQ ID NO:24) has certain amino acid sequence identity with the amino acid sequence of the protein designated "AB000628\_1" in the Dayhoff database. Accordingly, it is presently believed that PRO1927 disclosed in the present application is a newly identified member of the glycosyltransferase family of proteins and may possess glycosylation activity.

Please replace the paragraph beginning at page 108, line 28 of the substitute specification, with the following rewritten paragraph:

The starting material for the screen was genomic DNA isolated from a variety cancers. The DNA is quantitated precisely, e.g., fluorometrically. As a

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negative control, DNA was isolated from the cells of ten normal healthy individuals which was pooled and used as assay controls for the gene copy in healthy individuals (not shown). The 5' nuclease assay (for example, TaqMan™) and real-time quantitative PCR (for example, ABI Prizm 7700 Sequence Detection System™ (Perkin Elmer, Applied Biosystems Division, Foster City, CA)), were used to find genes potentially amplified in certain cancers. The results were used to determine whether the DNA encoding PRO1800, PRO539, PRO3434 or PRO1927 is over-represented in any of the primary lung or colon cancers or cancer cell lines or breast cancer cell lines that were screened. The primary lung cancers were obtained from individuals with tumors of the type and stage as indicated in ~~Table 6~~Table 7. An explanation of the abbreviations used for the designation of the primary tumors listed in ~~Table 6~~Table 7 and the primary tumors and cell lines referred to throughout this example are given below.

Please replace the paragraph beginning at page 110, line 12 of the substitute specification, with the following rewritten paragraph:

~~Table 6~~Table 7 describes the stage, T stage and N stage of various primary tumors which were used to screen the PRO1800, PRO539, PRO3434 and PRO1927 compounds of the invention.

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Please replace the table beginning at page 111, line 0 of the substitute specification, with the following rewritten table:

~~Table 6~~ Table 7  
Primary Lung and Colon Tumor Profiles

Primary Tumor Stage

	<u>Stage</u>	<u>Other Stage</u>	<u>Dukes Stage</u>	<u>T Stage</u>	<u>N Stage</u>
Human lung tumor AdenoCa (SRCC724) [LT1]	IIA			T1	N1
Human lung tumor SqCCa (SRCC725) [LT1a]	IIB			T3	N0
Human lung tumor AdenoCa (SRCC726) [LT2]	IB			T2	N0
Human lung tumor AdenoCa (SRCC727) [LT3]	IIIA			T1	N2
Human lung tumor AdenoCa (SRCC728) [LT4]	IB			T2	N0
Human lung tumor SqCCa (SRCC729) [LT6]	IB			T2	N0
Human lung tumor Aden/SqCCa (SRCC730) [LT7]	IA			T1	N0
Human lung tumor AdenoCa (SRCC731) [LT9]	IB			T2	N0
Human lung tumor SqCCa (SRCC732) [LT10]	IIB			T2	N1
Human lung tumor SqCCa (SRCC733) [LT11]	IIA			T1	N1
Human lung tumor AdenoCa (SRCC734) [LT12]	IV			T2	N0
Human lung tumor AdenoSqCCa (SRCC735)[LT13]	IB			T2	N0
Human lung tumor SqCCa (SRCC736) [LT15]	IB			T2	N0
Human lung tumor SqCCa (SRCC737) [LT16]	IB			T2	N0
Human lung tumor SqCCa (SRCC738) [LT17]	IIB			T2	N1
Human lung tumor SqCCa (SRCC739) [LT18]	IB			T2	N0
Human lung tumor SqCCa (SRCC740) [LT19]	IB			T2	N0
Human lung tumor LCCa (SRCC741) [LT21]	IIB			T3	N1
Human lung AdenoCa (SRCC811) [LT22]	IA			T1	N0
Human colon AdenoCa (SRCC742) [CT2]	M1	D	pT4	N0	
Human colon AdenoCa (SRCC743) [CT3]		B	pT3	N0	
Human colon AdenoCa (SRCC744) [CT8]		B	T3	N0	
Human colon AdenoCa (SRCC745) [CT10]		A	pT2	N0	
Human colon AdenoCa (SRCC746) [CT12]	MO, R1	B	T3	N0	
Human colon AdenoCa (SRCC747) [CT14]	pMO, RO	B	pT3	pN0	
Human colon AdenoCa (SRCC748) [CT15]	M1, R2	D	T4	N2	
Human colon AdenoCa (SRCC749) [CT16]	pMO	B	pT3	pN0	
Human colon AdenoCa (SRCC750) [CT17]		C1	pT3	pN1	
Human colon AdenoCa (SRCC751) [CT1]	MO, R1	B	pT3	N0	
Human colon AdenoCa (SRCC752) [CT4]		B	pT3	M0	
Human colon AdenoCa (SRCC753) [CT5]	G2	C1	pT3	pN0	
Human colon AdenoCa (SRCC754) [CT6]	pMO, RO	B	pT3	pN0	
Human colon AdenoCa (SRCC755) [CT7]	G1	A	pT2	pN0	
Human colon AdenoCa (SRCC756) [CT9]	G3	D	pT4	pN2	
Human colon AdenoCa (SRCC757) [CT11]		B	T3	N0	
Human colon AdenoCa (SRCC758) [CT18]	MO, RO	B	pT3	pN0	

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Please replace the paragraph beginning at page 113, line 34 of the substitute specification, with the following rewritten paragraph:

The PRO1800, PRO539, PRO3434 and PRO1927 compounds of the invention were screened in the following primary tumors and the resulting  $\Delta C_t$  values greater than or equal to 1.0 are reported in ~~Table 7~~Table 8 below.

Please replace the table beginning at page 114, line 0 of the substitute specification, with the following rewritten table:

~~Table 7~~Table 8 ( $\Delta C_t$  values in lung and colon primary tumor models)

<u>Primary Tumor</u>	<u>PRO1800</u>	<u>PRO539</u>	<u>PRO3434</u>	<u>PRO1927</u>
LT11	1.65, 1.59, 1.03			
LT12	1.34, 2.28, 2.03	1.25		
LT13	1.27, 2.18	1.64, 1.08	5.24, 4.47	4.38, 4.80
LT15	1.70, 2.23, 1.93	1.78, 1.10	1.24	1.00
LT16	1.00, 1.05, 1.09		3.65, 3.19	2.73, 2.74
LT17	1.94, 1.63	1.94, 1.01		
LT18	1.12			
LT19	2.51, 2.18	1.16		
LT21	1.30	1.32		
CT2	1.50			
CT3		1.17		
CT10		1.16		
CT12		1.19		
CT14	1.62			
CT15	1.48, 1.08	1.03	1.19, 1.40	1.10, 1.30
CT5	1.10			
CT11	1.20	1.12		
Colo-320 (colon tumor cell line)	1.16		1.78, 1.76, 1.74	1.51
HF-00084 (lung tumor cell line)			2.20	2.41
HCT-116 (colon tumor cell line)			2.15, 2.22	1.41, 1.47
HF-00129 (lung tumor cell line)			1.00, 1.17, 4.64	2.31, 5.14
SW-620 (colon tumor cell line)			1.11	2.40
HT-29 (colon tumor cell line)			1.30	
SW-403 (colon tumor cell line)			1.64	
LS174T (colon tumor cell line)			1.75	
HCC-2998			1.42	
			1.15	

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(colon tumor cell line)	
A549	1.51, 1.09
(lung tumor cell line)	
Calu-6	1.60, 1.22
(lung tumor cell line)	
H157	1.61
(lung tumor cell line)	
H441	1.07, 1.15
(lung tumor cell line)	
H460	1.01
(lung tumor cell line)	
SKMES1	1.02
(lung tumor cell line)	
H810	1.20, 1.54
(lung tumor cell line)	



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Please replace the paragraph beginning at page 127, line 6 of the substitute specification, with the following rewritten paragraph:

These deposits were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit, and at least five (5) years after the most recent request for the furnishing of a sample of the deposit was received by the depository. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC. 122 and the Commissioner's rules pursuant thereto (including 37 CFR. 1.14 with particular reference to 886 OG 638).